Modern Concepts of Cardiovascular Disease

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RECENT ADVANCES IN THE PHYSIOLOGY OF THE CORONARY CIRCULATION

Recent studies of the heart have given rise to several new anatomical and functional concepts concerning the coronary venous system, collaterals, response of the heart to increased load and nerve stimulation, all of which materially modify our working knowledge of the coronary circulation. In large part, these have been made possible by the introduction of new methods, instruments and new or modified experimental procedures.

The vascular beds supplied by the right and left coronary arteries are predominantly located in the right auricle and ventricle, and in the left auricle and ventricle respectively. However, adjacent portions of the two ventricles are supplied in varying amounts by both coronary arteries.

Small arterial communications normally exist between the right and left coronary arteries, between branches of the same coronary artery and between the coronary and extracardiac arteries. Following chronic occlusion of a coronary artery or its branches, gross evidence of development of inter-arterial collaterals has been shown radiographically with opaque injection material. An indication of intercoronary collateral development can be demonstrated experimentally by the measurement of the retrograde flow of blood from a severed main coronary branch. In acute and chronic occlusion experiments with otherwise normal hearts, the retrograde flow is at first small, but this increases within a few hours, becomes considerably greater within a few days, and approximates in days to weeks the pre-occlusion value for the normal rate of inflow to that branch. This process is slow relative to that found in other less vital body regions. If, presumably, the intracardiac sources of blood supply are insufficient, extracardiac anastomoses also become evident and sizeable external communications can be demonstrated.

The coronary sinus and associated veins emptying near its mouth constitute the major superficial drainage system of the left heart. Measurements of coronary sinus outflow have been used in the past to indicate quantitative and directional changes in total coronary inflow. Considerable controversy has arisen as to the validity of this practice but the arguments are supported by observation made with the heart-lung or isolated heart preparation. It is probable that a more consistent and reliable evaluation of the coronary inflow-coronary sinus outflow relationship could be made with a less artificially controlled preparation which was permitted to retain a more nearly normal state of hemodynamics. However, from the practical experimental standpoint, the issue would seem to be of little import since there are now available adequate and simple methods of directly measuring coronary inflow in a somewhat more reliable preparation.

The venous drainage of the right ventricle is largely by way of the anterior cardiac veins to the right atrium. Until recently, this system of superficial veins over the surface of the right heart had been virtually ignored. Experimentally, cannulation of only the major anterior cardiac veins has permitted recovery of from 50-92% of the blood entering the right coronary artery. These percentages are considered minimal, since for technical reasons, no attempts were made to quantitate the flow from the smaller anterior cardiac veins, the right auricular veins and the many small veins emptying into the great cardiac vein, all of which constitute channels of exit for blood supplied to the right heart by the coronary artery. Thus, the major venous drainage of each heart is by way of its own system of superficial veins.

Histological studies of serial sections, reconstruction, dye injections and perfusion experiments of the isolated heart have demonstrated the presence and distribution of Thebesian and luminal vessels through which the coronary vessels communicate with the atrial and ventricular chambers of the heart. These channels are much more abundant in the right ventricle. It is conceivable that they could function in the normal heart and that their role could be quite important, particularly to the right ventricle in the presence of superficial coronary vein occlusion, and to the left ventricle during left coronary artery occlusion. However, although many experiments have been devised to determine if, when, in which direction and to what extent blood flows through these channels, none has been sufficiently conclusive to justify more than a speculation as to whether they ever function in the heart beating *in situ*. From the standpoint of the normal heart, the critical objections to these experiments can be resolved into either (1) the false assumption that all blood leaving the right auricle and the right ventricle, exclusive of that entering from the coronary sinus and venae cavae, has its origin in the Thebesian vessels, thereby ignoring the considerable inflow through the anterior cardiac veins, or (2) the establishment of decidedly abnormal pressure gradients between coronary vessels and the chambers of the heart for the purpose of demonstrating the existence, direction and magnitude of Thebesian flow. Their functional role in long sustained coronary artery or coronary vein occlusion cannot be determined until the utilization of extracardiac arterial and venous collateral communications has been excluded.

The determinants of blood flow through the coronary circuit are physical and chemical in nature. For all or any portion of the vascular bed, flow will vary directly with the pressure head and inversely with the viscous resistance encountered in transit through

the bed, and the pressure at the end of the circuit. Aortic blood pressure determines the head applied at the coronary ostia, and right auricular pressure at the points of entry of the anterior cardiac veins and coronary sinus largely determines the venous back pressure. Viscous resistance to flow is governed for the most part by the bore of the blood vessels which in turn can be modified by two factors, (1) passive compression and relaxation resulting from rhythmic myocardial contraction (extravascular support), (2) active vasomotor changes in the vessels induced by nervous and humoral influences upon their intrinsic muscles. Although the extent to which each of the flow determinants contributes to the observed change in coronary flow is often impossible to determine, qualitative and directional changes can frequently be identified. Recent refinements in methods and preparations have permitted conclusions which place greater emphasis upon the importance of alterations in cardiac metabolism as a regulator of coronary flow.

Of particular interest has been the subject of increased cardiac load versus coronary flow. The bulk of the evidence, as derived in the past from heart-lung and comparable preparations, has formed the basis for the conclusion that augmentation of the load on either ventricle by constriction of the pulmonary artery or aorta (central to the coronary orifices) decreases coronary blood flow to the corresponding ventricle. The decrease in flow is attributed to the dominant effect of the direct mechanical inhibitive action of the increased vigor of the heart. Such a response would not appear as advantageous to the heart. In recent studies with hearts beating *in situ* under more nearly normal physiological conditions, either right or left coronary flow increased considerably upon elevation of right or left ventricular pressure; measurement of cardiac output and oxygen consumption has demonstrated an increase in the work and metabolism of the heart. Although the mechanism for the increase in coronary flow cannot be identified with certainty in these experiments, it would seem probable that a local increase in metabolites is responsible for the coronary dilatation. In all events, these hearts have at their disposal a compensatory means by which their blood supply can, at least in part, be adjusted to the work and metabolic requirements. The flow-promoting mechanism can be shown to be antagonized by a flow-limiting mechanism. For example, if in the presence of an adequately maintained central coronary pressure, the pulmonary artery constriction and release is abrupt, the sustained flow increase observed above is preceded and followed by a short period of flow reduction and elevation respectively whose beginning is coincident with the time of sudden constriction and release of the pulmonary artery. These abrupt changes in flow coincident with the onset of elevation and reduction in right ventricular pressure can be regarded as evidence of the temporary separation of the influence of change in extravascular support on flow, while the sustained flow increase between these periods indicates the dominant influence of coronary dilatation over the effects of extravascular support. If the experiments are intentionally prolonged (4-5 hours), the right coronary flow response to pulmonary artery constriction ultimately becomes a sustained decrease which returns to the control level upon release of the pulmonary artery. Thus, in the later stages of an experiment in which the condition of the heart *in situ* is certainly far removed from normal, the flow reducing effect of increased extravascular support is dominant over whatever flow-promoting mechanism the heart has still retained. As measured under these conditions and by others using the heart-lung preparation, the observed decrease in coronary flow cannot be regarded as the normal response to an increased cardiac load.

The regulating influence of sympathetic nerves upon the coronary circulation has also been a subject of considerable study. With the use of various preparations and methods, previous investigators have reported that coronary flow increases — or that it decreases as the result of stimulation of the same nerves. It is significant that in no instance in the past has coronary *inflow* been measured with the heart beating *in situ* by any method. Studies with the fibrillating heart have been presented to support the view generally held that the changes in coronary inflow are primarily attributable to direct nerve action upon the coronary vessels. Although the possibility cannot be denied that a direct vasomotor influence exists, its demonstration in the fibrillating (or normally) beating heart rests upon the unverified assumption that nerve stimulation leaves unaltered the vigor of the normal or fibrillary contractions and the metabolism of the heart. More recently, in dogs in which the heart had been left undisturbed (except for insertion of a rotameter in the coronary circuit), stimulation of the stellate ganglia or their cardiac branches consistently gave rise to an increase in coronary flow. Although an increase in heart rate and aortic blood pressure, singly or together, can be shown to be not indispensible factors, an increase in coronary flow has never been observed without evidence of increased cardiac work and/or increased cardiac metabolism. Hence, it is not improbable that stimulation of these sympathetic structures increases, by some as yet unknown mechanism, the work done by the heart, resulting in an increase in metabolism and elaboration of metabolites; the latter could, by acting locally upon the coronary vessels, cause active dilatation and therefore an increase in coronary flow. This physiological train of events is not dissimilar to that discussed above in relation to increasing the work of the heart by increasing its load.

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